



Predicting an Individual's Physiologic State without a Crystal Ball

Jaques Reifman, Ph.D.

Senior Research Scientist (ST)

4th Infantry Division and Materiel Command

ATA, TATRC Partnership Series

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BIC/BHSAI

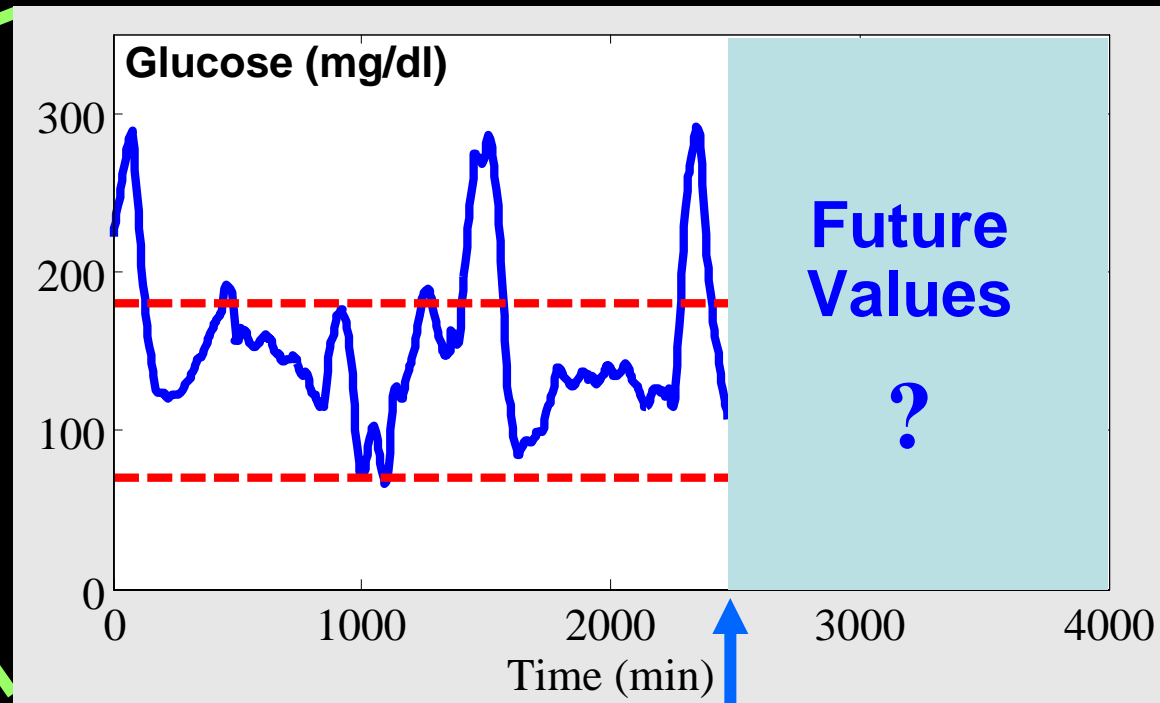


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Knowing the Past is Good, but Knowing the Future is even Better: **Predictive Models!**

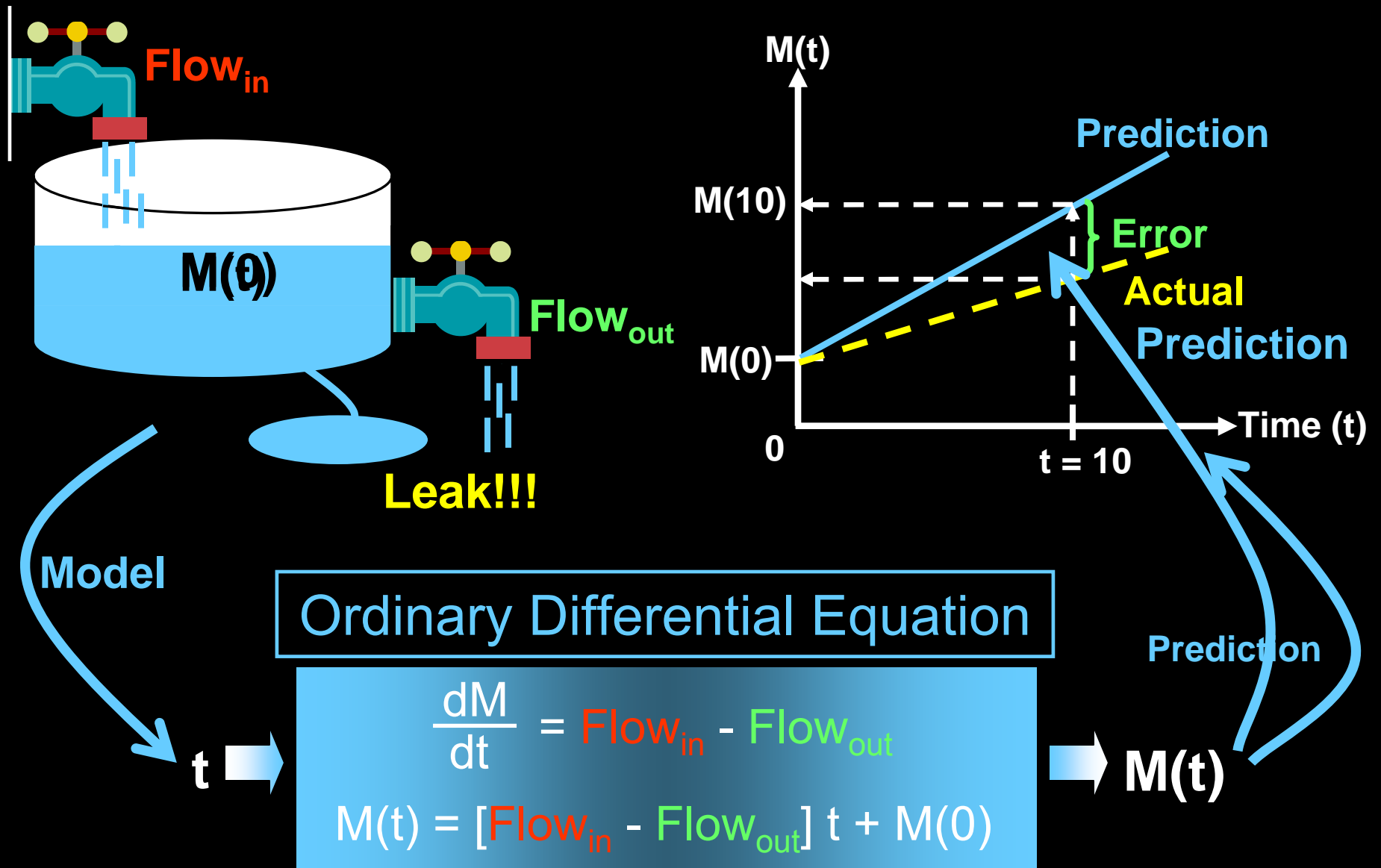


present time

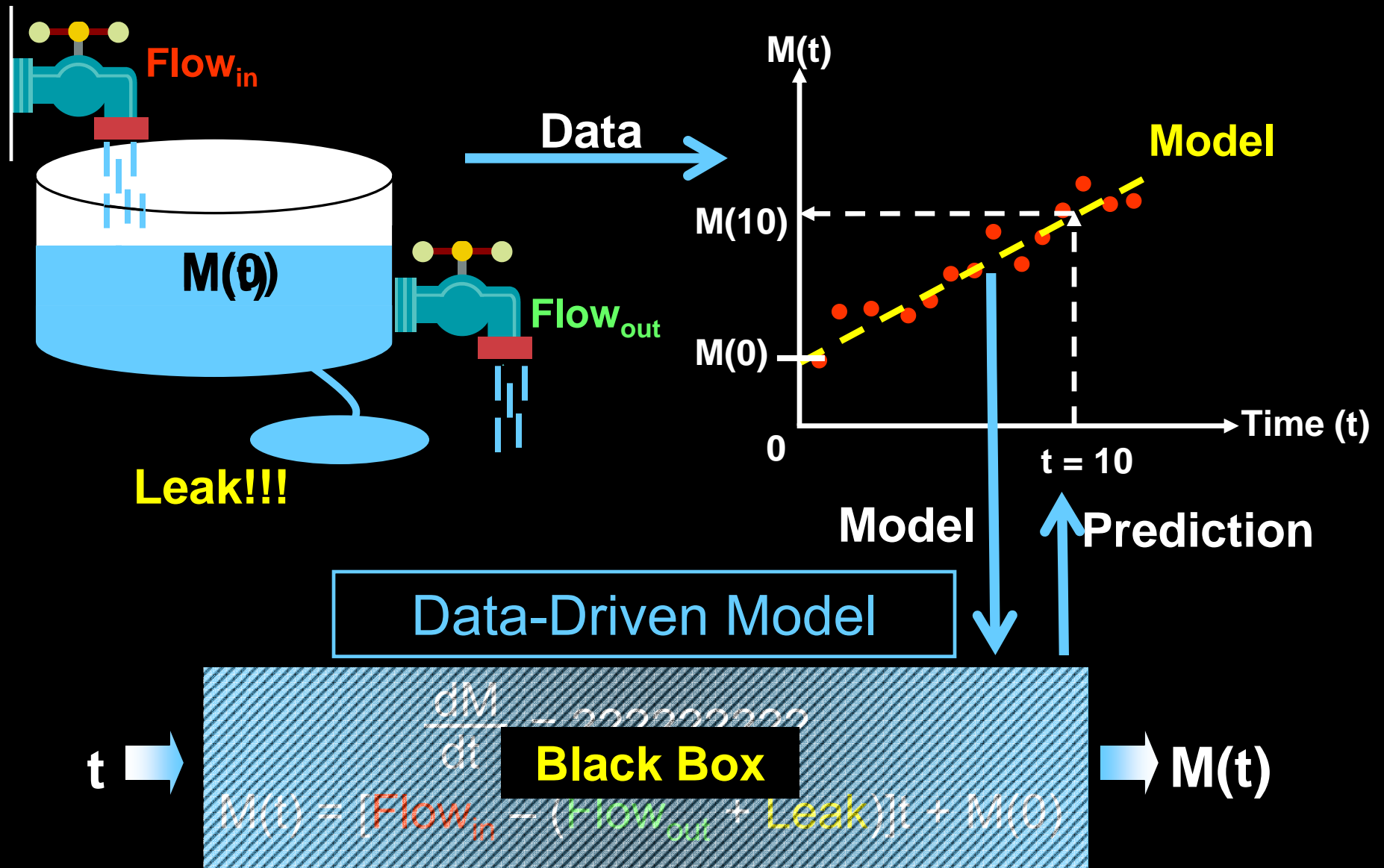
Biomathematical Models

- **First-Principles Models** (physiology based)
- **Data-Driven Models** (derived from data)

First-Principles Model



Data-Driven Model



Model Requirements for Practical Use

- **Highly accurate (for a reasonable horizon)**

⇒ Individual-specific models

- **Minimum manual tuning**

⇒ Adaptive first-principles models

⇒ “Universal” data-driven models

- need to measure “something” from the individual -

Physiologic Variables (or States) We Wish to Predict

1. Performance impairment due to total sleep loss

2. Body core temperature (minimize heat injuries)

*- Armed forces (2003-2005)[†]: 3617 heat exhaustion injuries
784 heat stroke injuries*

3. Glucose concentrations (diabetic patients)

*- \$1 in every \$10 health care dollars is attributed to diabetes**

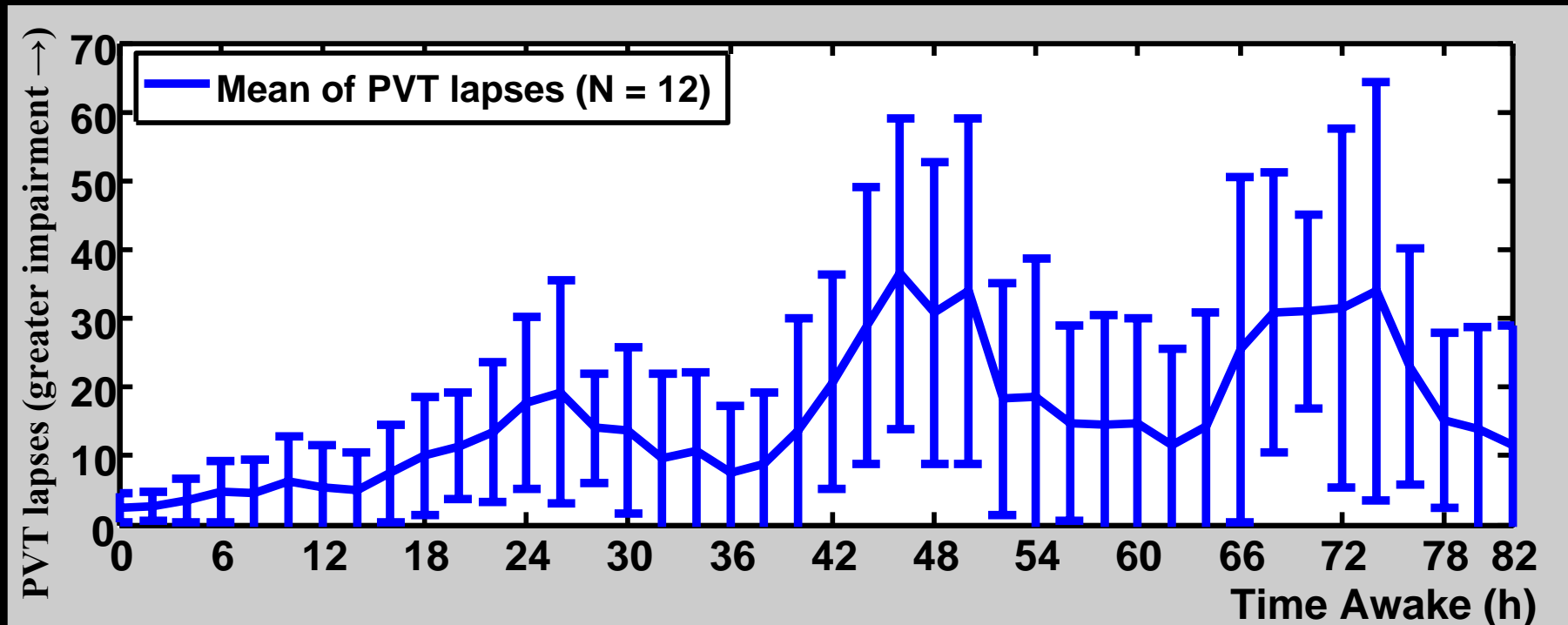
[†]chppm-www.apgea.army.mil/heat/

*Hogan et al., *Diabetes Care*, **26**, 917 (2003)

Performance Impairment Prediction

Problem: Predict performance impairment due to total sleep loss (82-hour study of total sleep deprivation)*

Measure of Performance: Lapses in a reaction-time test (Psychomotor Vigilance Task – PVT) every two hours



*Wesensten et al., *J. Sleep Res*, 14, 255 (2005)

Data from Tom Balkin's group (Walter Reed)

PVT lapses: # of times reaction time > 500 msec over a 10-min test session

Two-Process Model of Sleep Regulation*

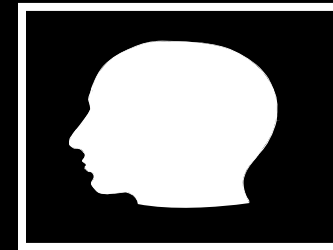
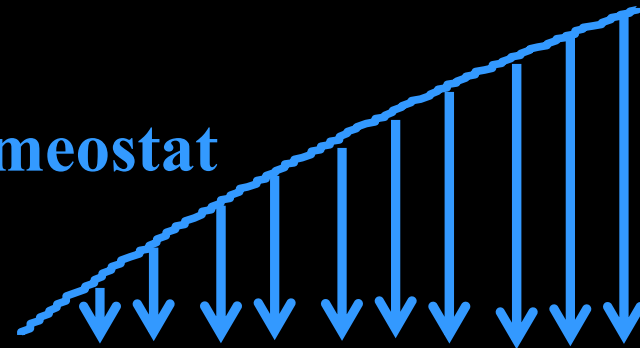
- “state-of-the-art” first-principles model -

Process S

(sleep/wake history)

$$S(t) = 1 - \exp(-\Delta t / \tau_r)(1 - S(t-1))$$

Homeostat

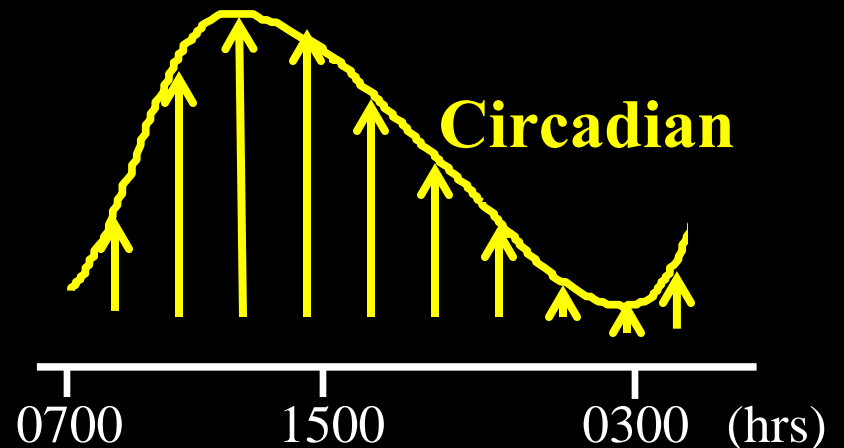


Process C

(biological clock)

$$C(t) = \sum_{i=1}^5 a_i \sin\left(\frac{2i\pi}{\tau}(\Delta t(t-1) + \phi)\right)$$

Circadian



*Borbély, *Human Neurobiol.*, 1, 195 (1982)

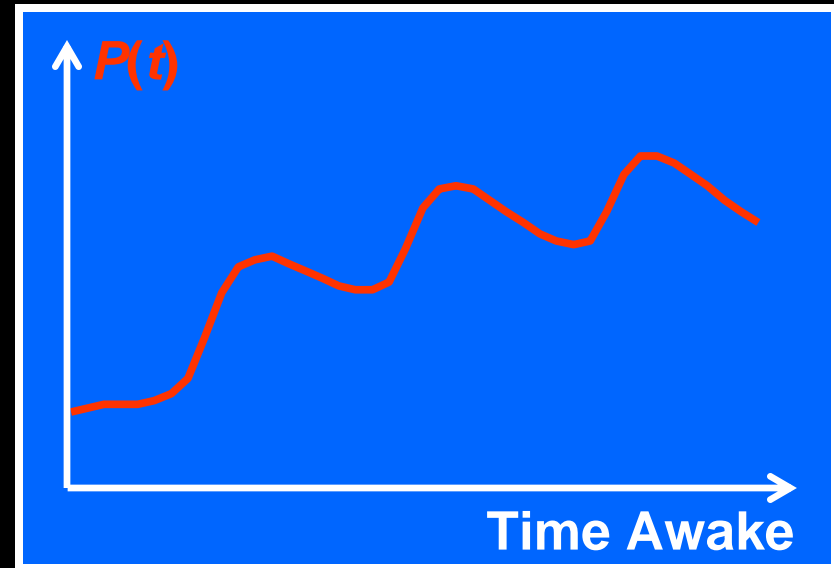
Predicting Performance Using the Two-Process Model

Performance $P(t)$:

$$P(t) = S(t) + C(t)$$

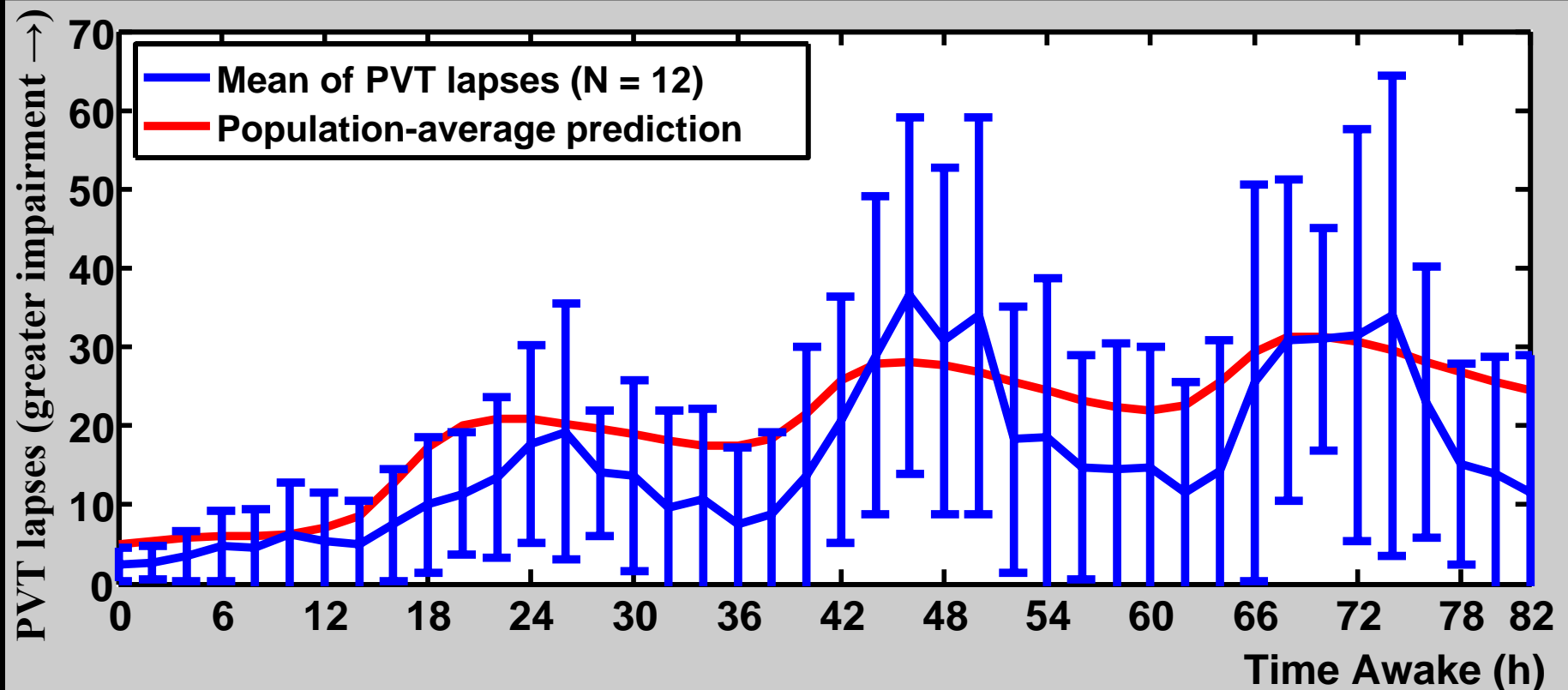
For total sleep deprivation:

$$P(t) = \alpha - \alpha S(0) \gamma^{t-1} + \beta \sum_{i=1}^5 a_i \sin[i\omega((t-1)\Delta t + \phi)]$$



Population-Avg. Solution: Model parameters (τ_r , $S(0)$, α , β , ϕ) are fixed

Population-Avg. Model Not Optimal



Solution: Individual-specific adaptive models

- Models parameters (τ_r , $S(0)$, α , β , ϕ ,) are automatically adjusted, for each individual, after each PVT observation

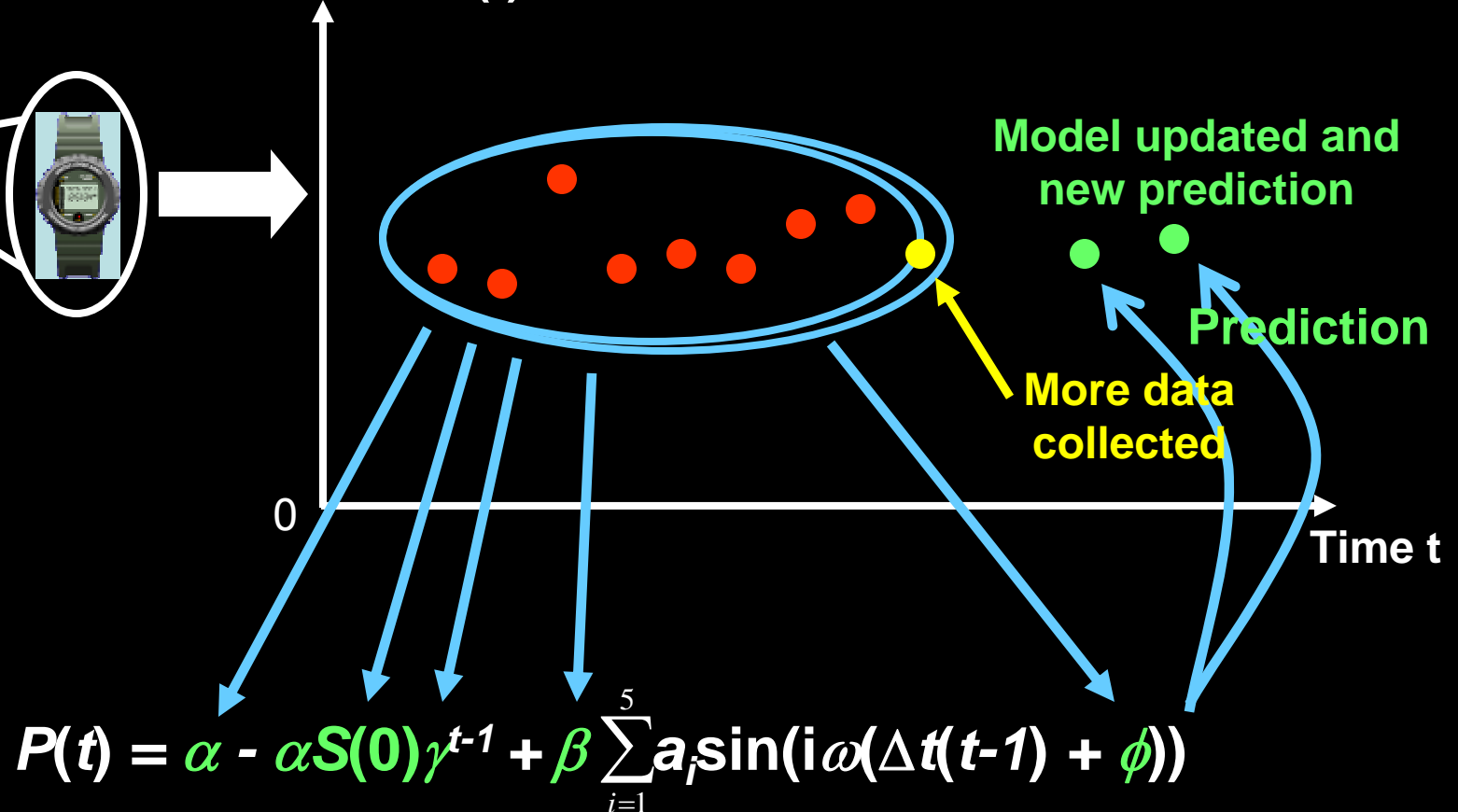
First-Principles, Two-Process Model

- Adaptive, Individual-Specific Model -

Sleep-Deprived
Soldier



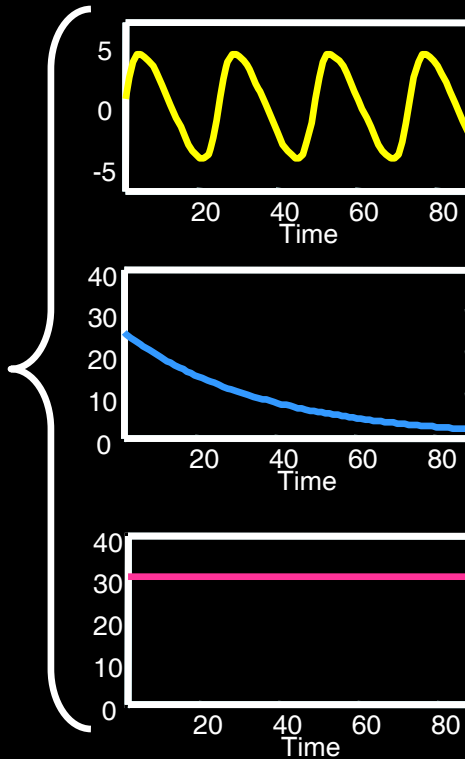
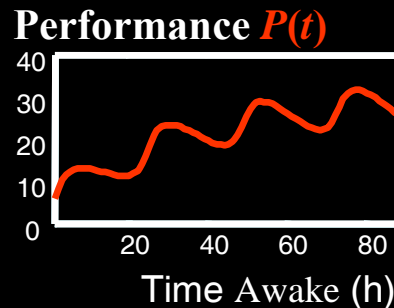
Performance $P(t)$



Adaptive Individual-Specific Models*

Performance (P):

$$P(t) = \alpha - \alpha S(0) \gamma^{t-1} + \beta \sum_{i=1}^5 a_i \sin(i \omega (\Delta t(t-1) + \phi))$$



Parameters Estimated

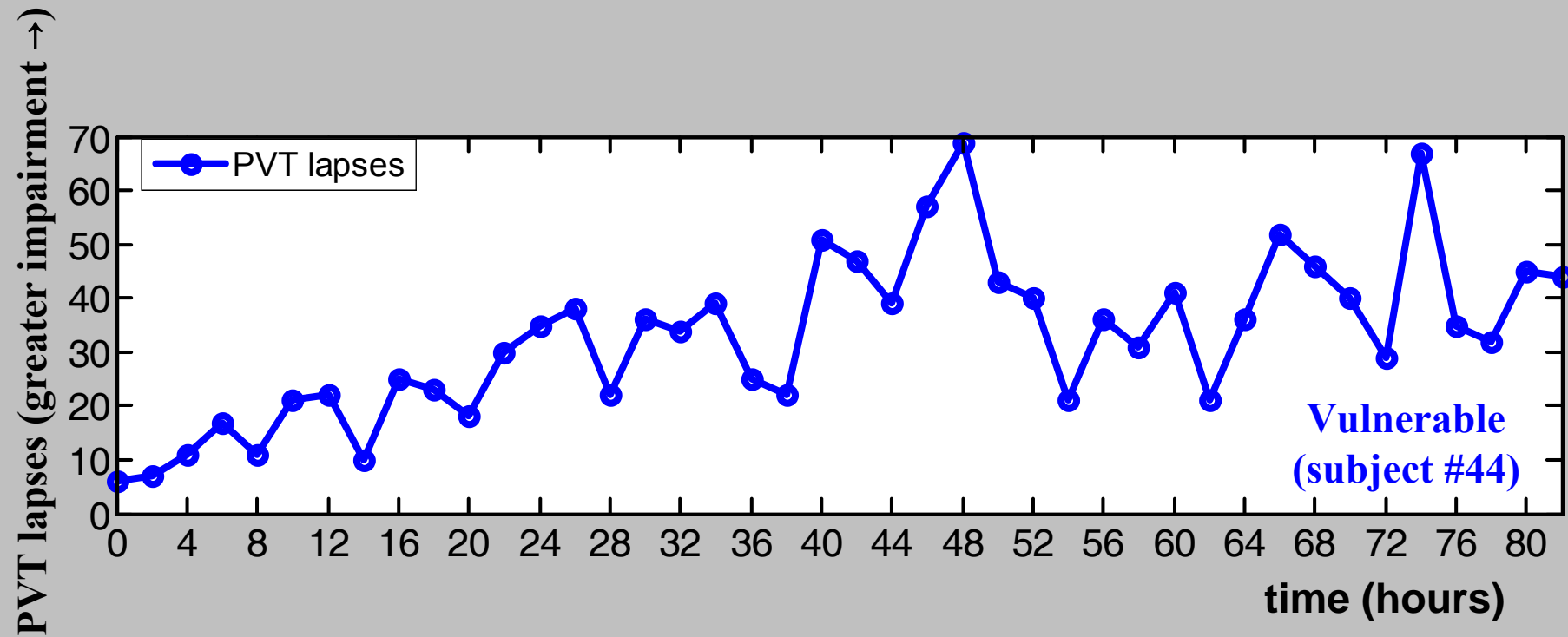
β and ϕ

$\alpha S(0)$ and γ

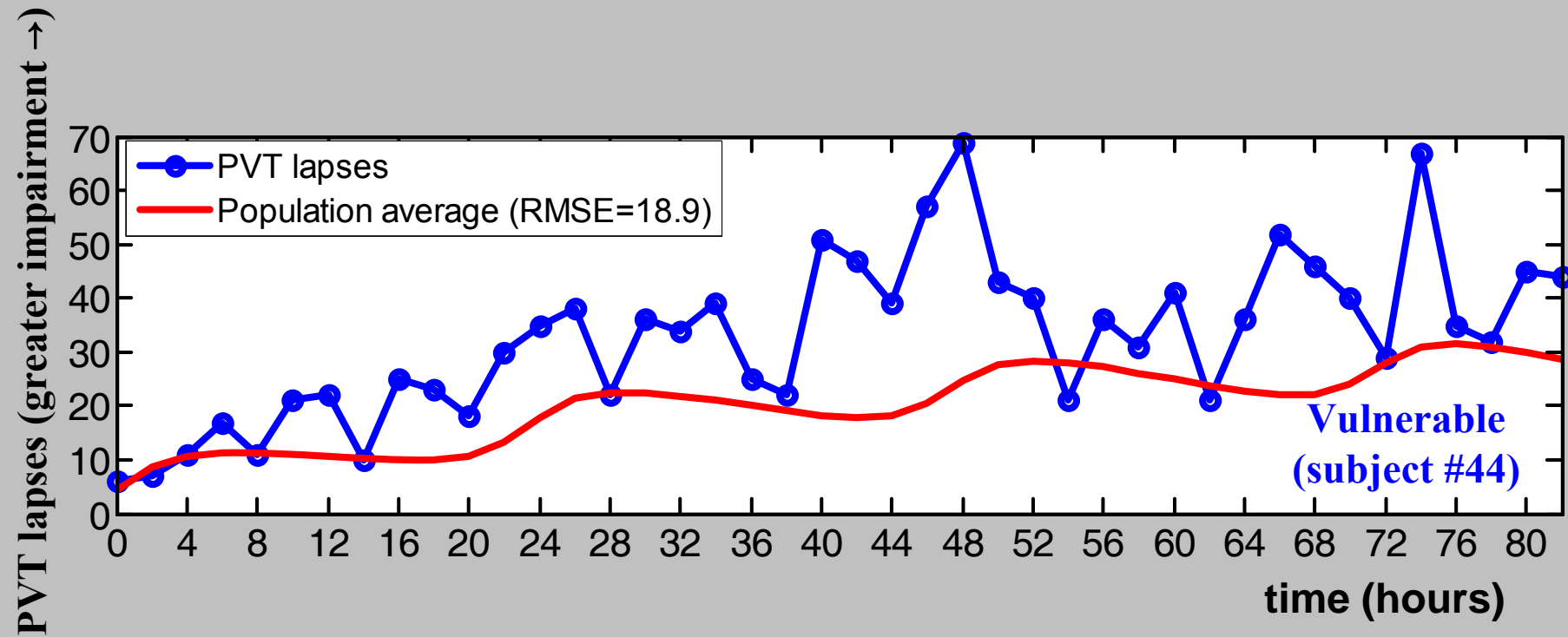
α

* Rajaraman et al., *J Appl Physiol.*, **104**, 459 (2008)

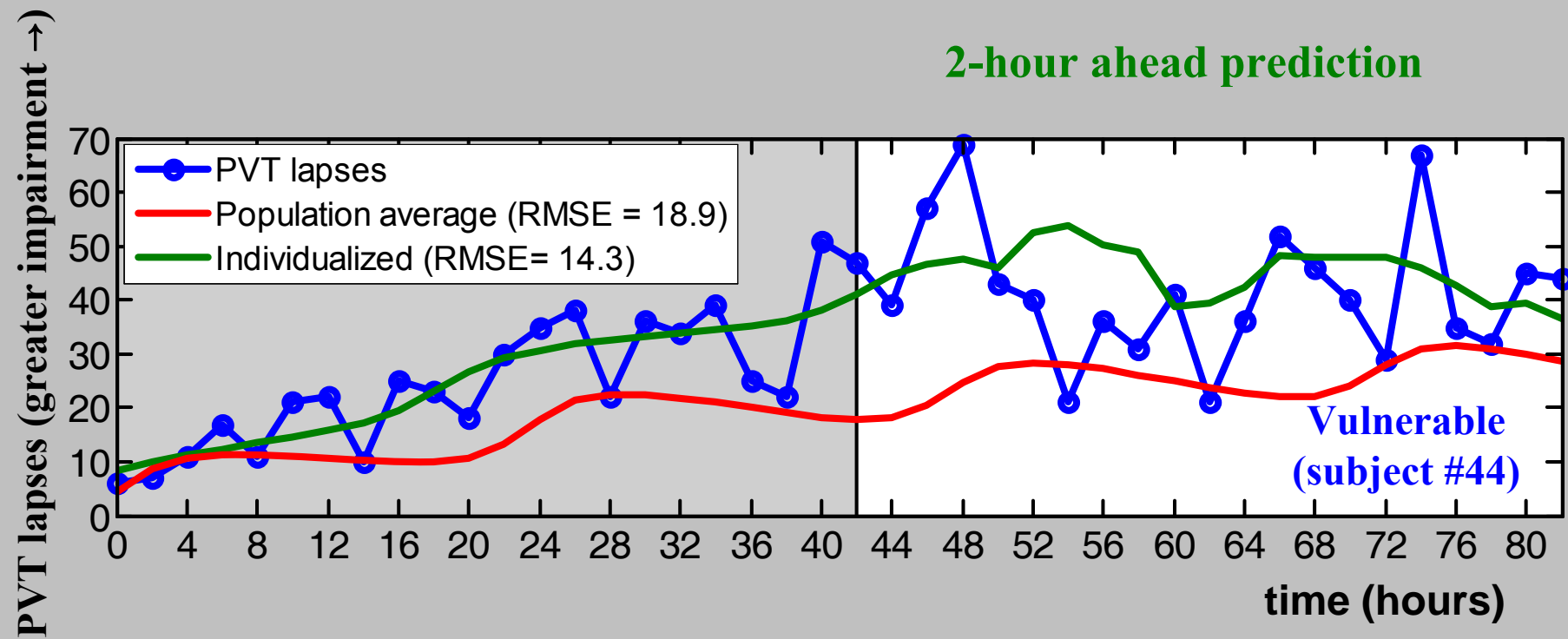
Predicting a Vulnerable Subject



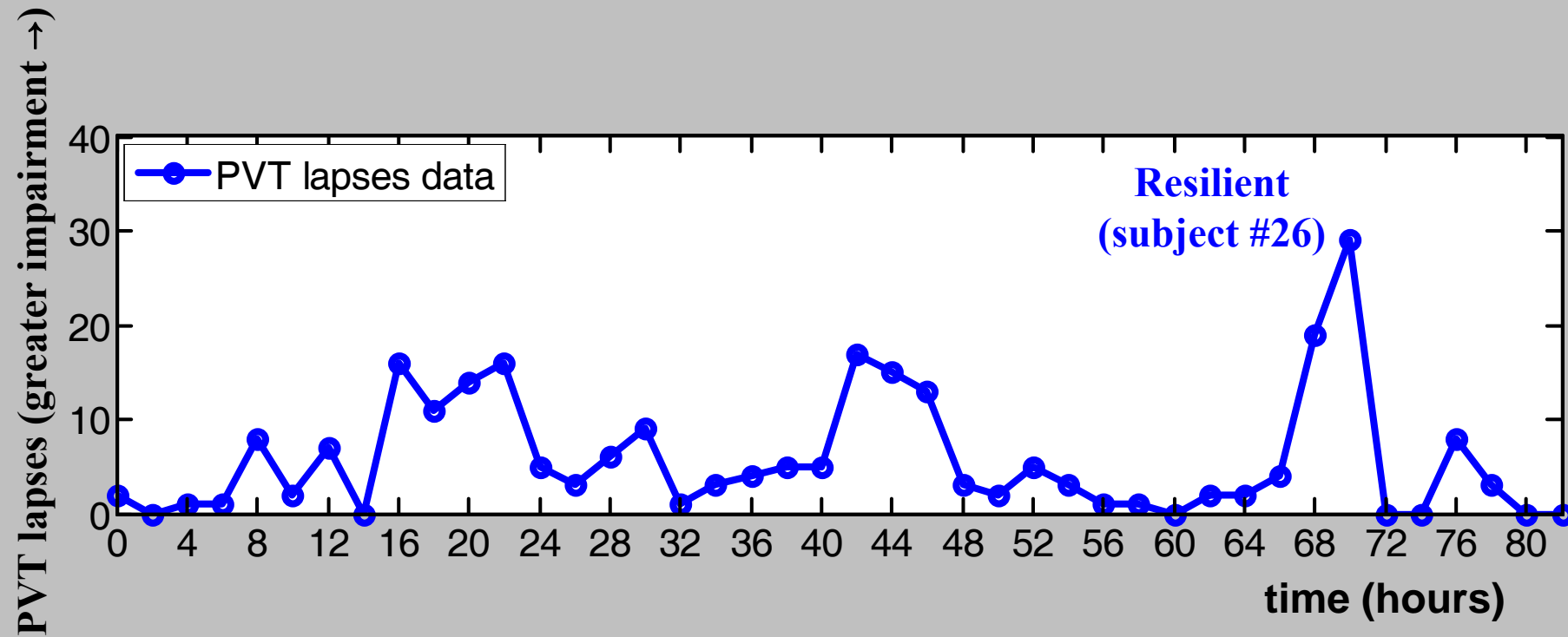
Population-Average Prediction



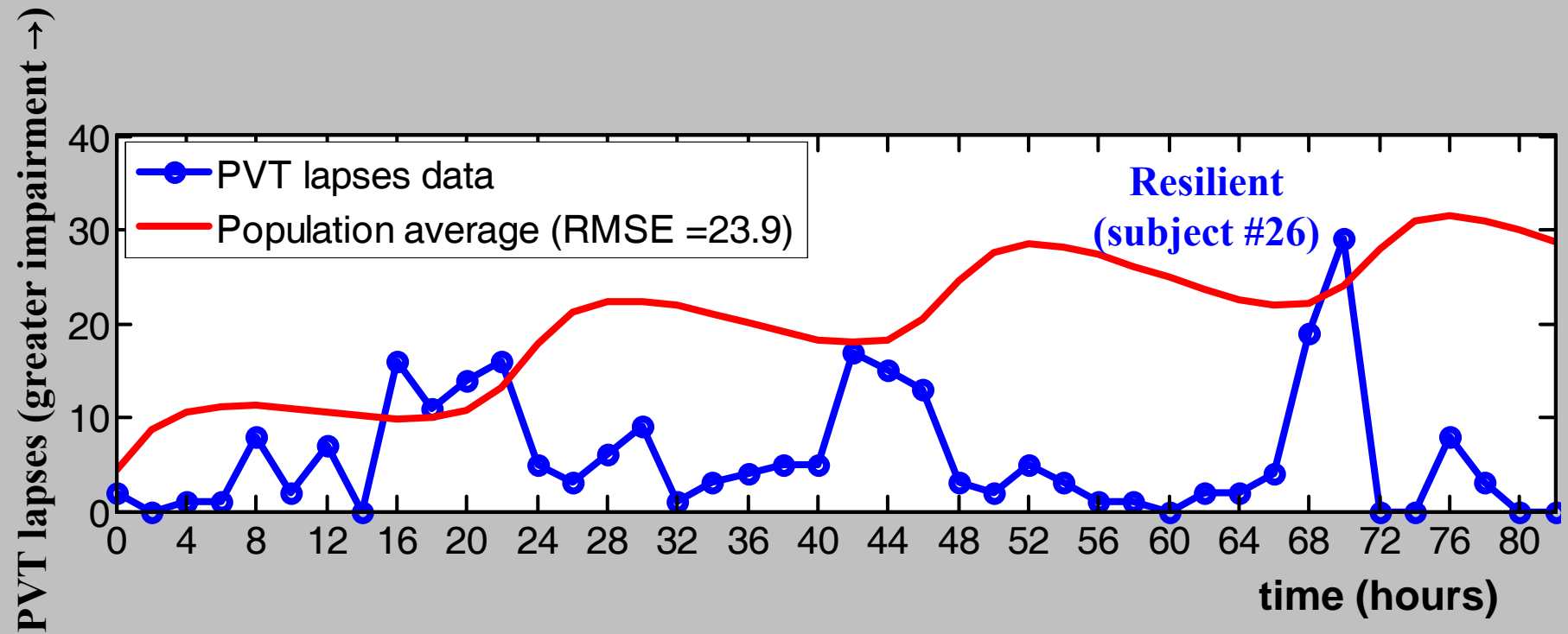
Individualized vs. Population-Average Predictions



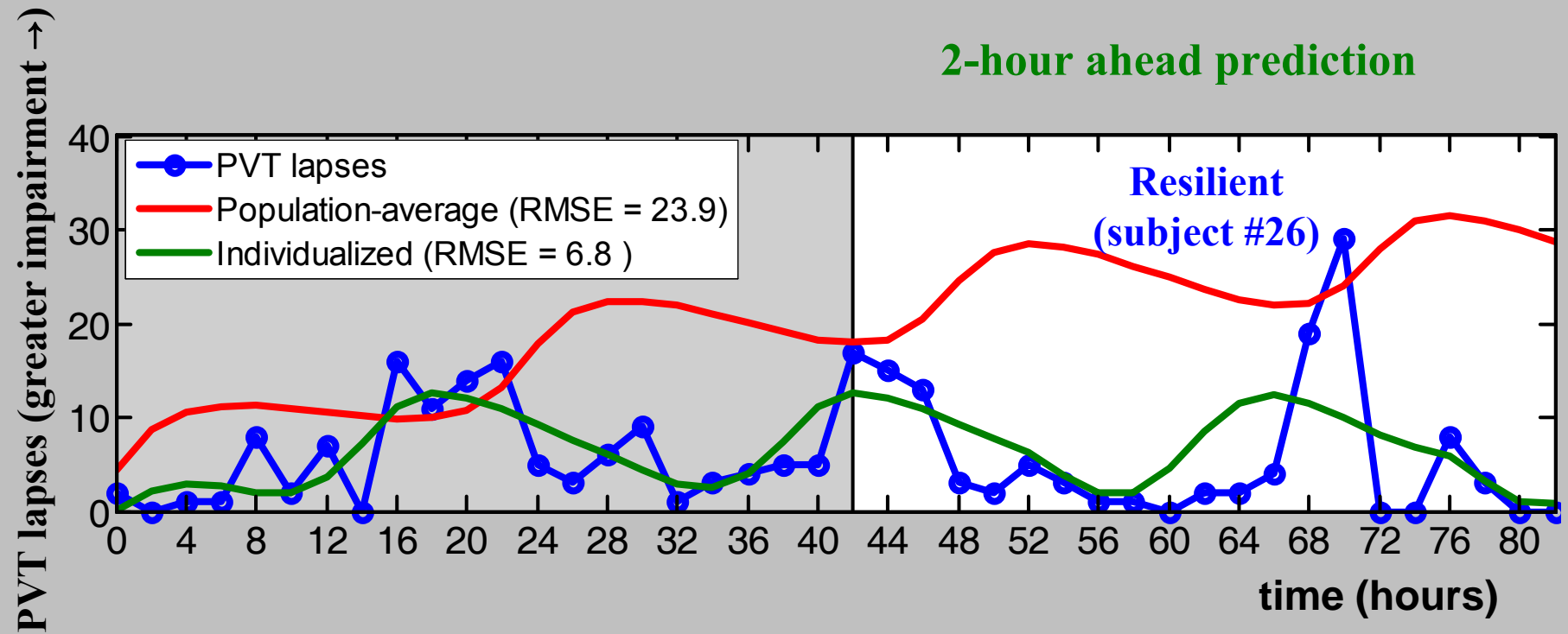
Predicting a Resilient Subject



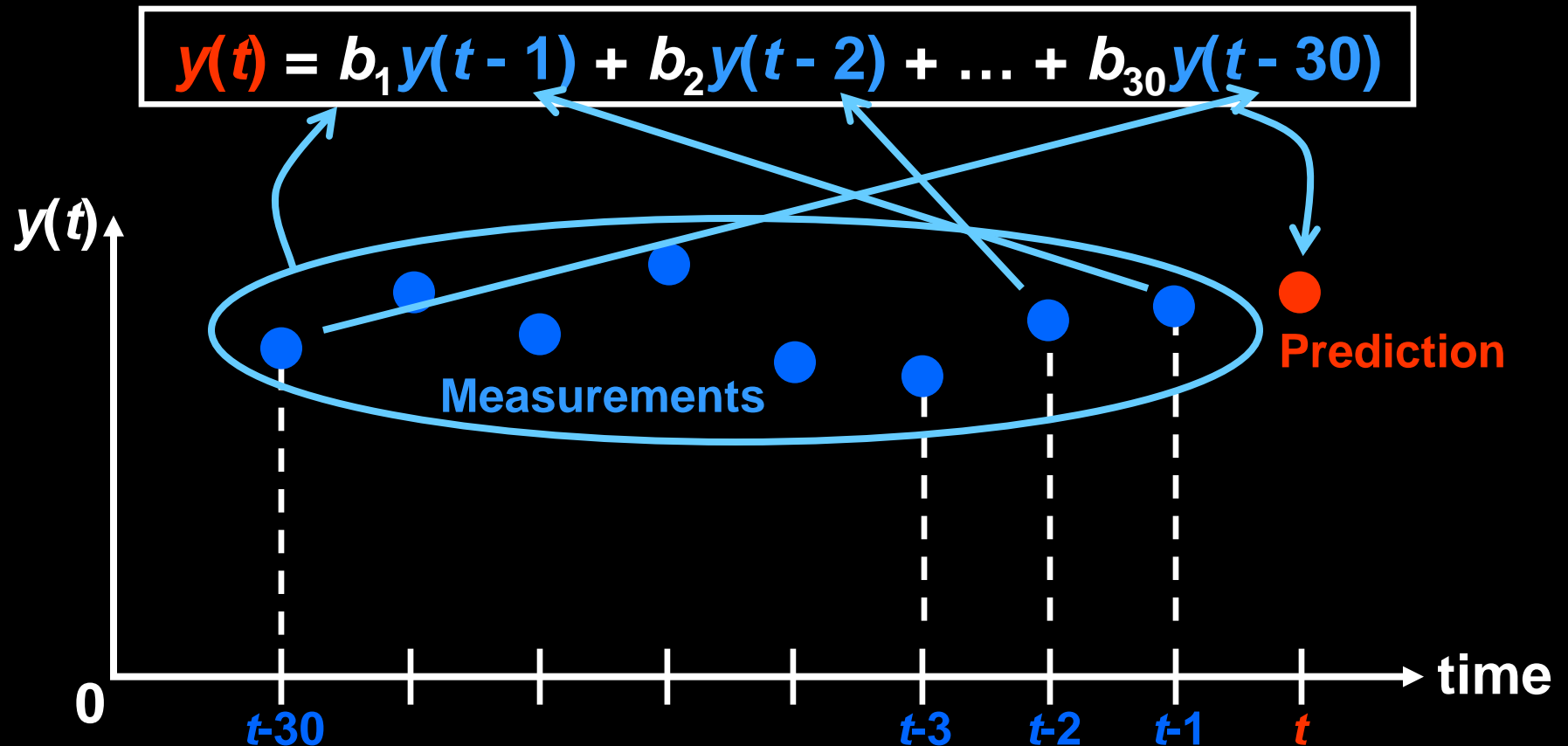
Population-Average Prediction



Individualized vs. Population-Average Predictions



Autoregressive (AR), Data-Driven Model



$y(t)$: measurement/prediction at time t

b_i : model coefficients (unknown)

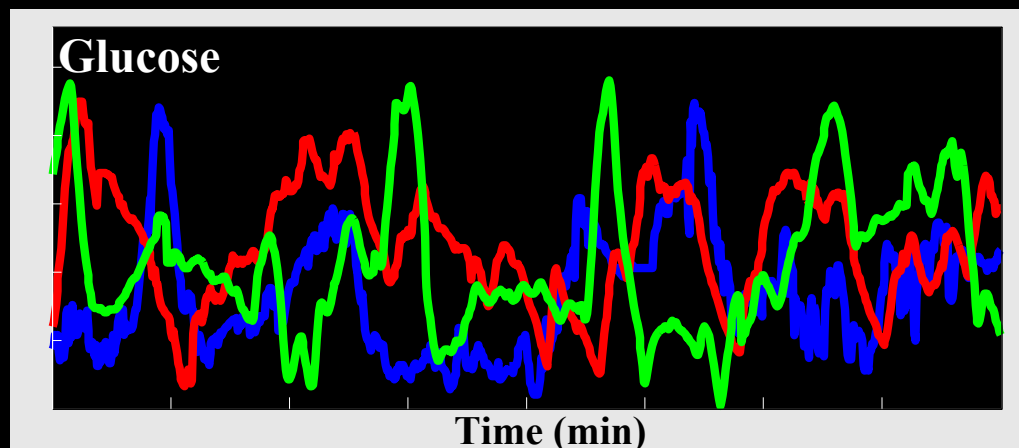
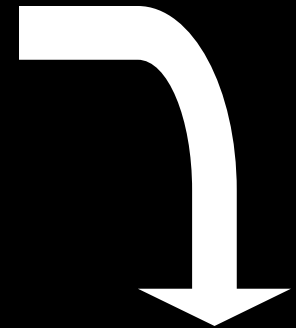
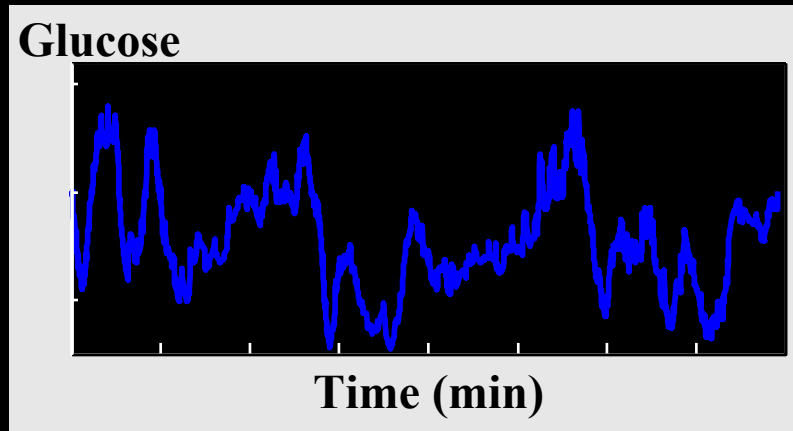
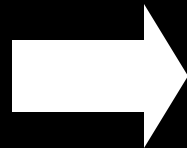
30: number of previous measurements

Found to be individual independent!!!

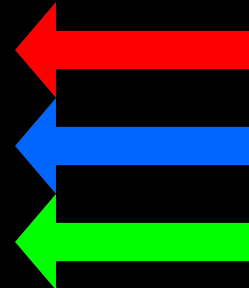
Autoregressive (AR), Data-Driven Model

- "Universal," Individual-Independent Model -

Continuous Glucose Monitor



Predictions



**Data-Driven,
Universal
Model (fixed
coefficients b_i)**

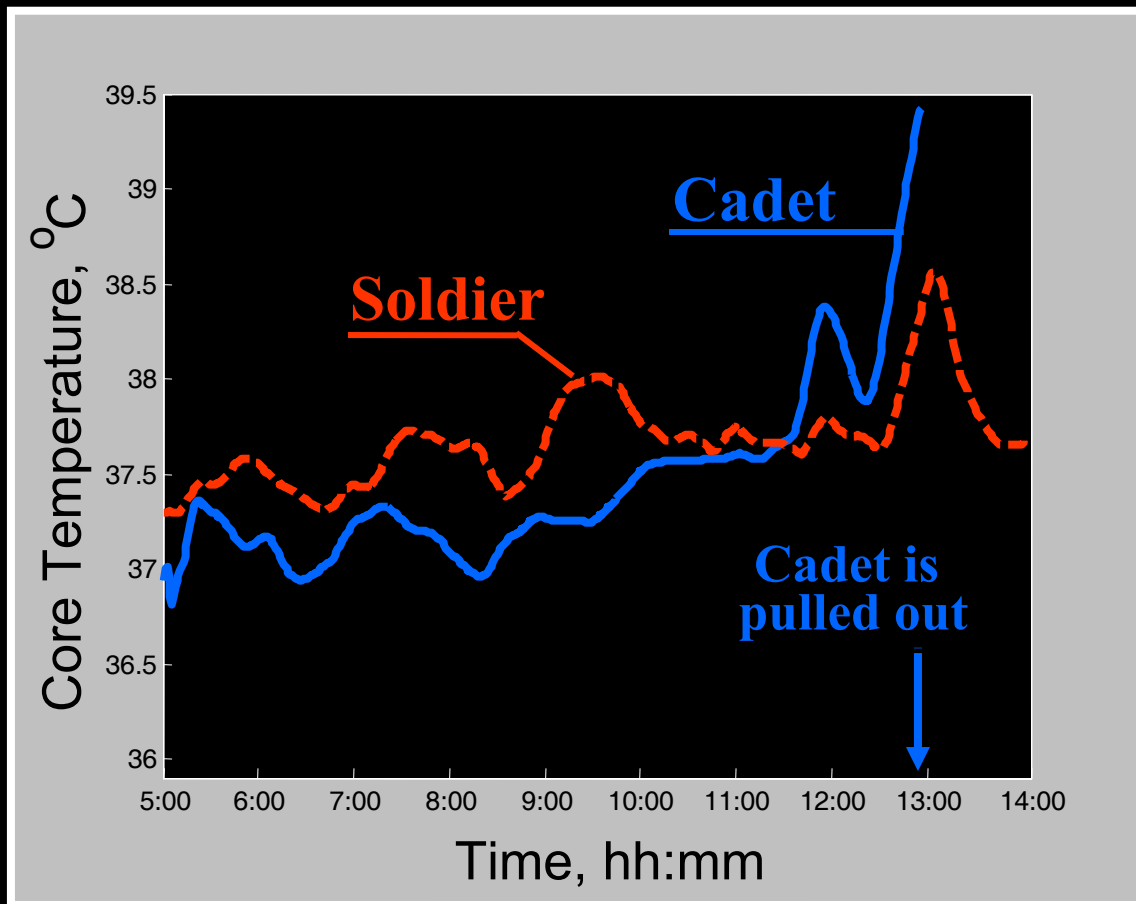
Glucose
Measurements



Body Core Temperature Prediction

Problem: Predict core temperature 20-minutes ahead*

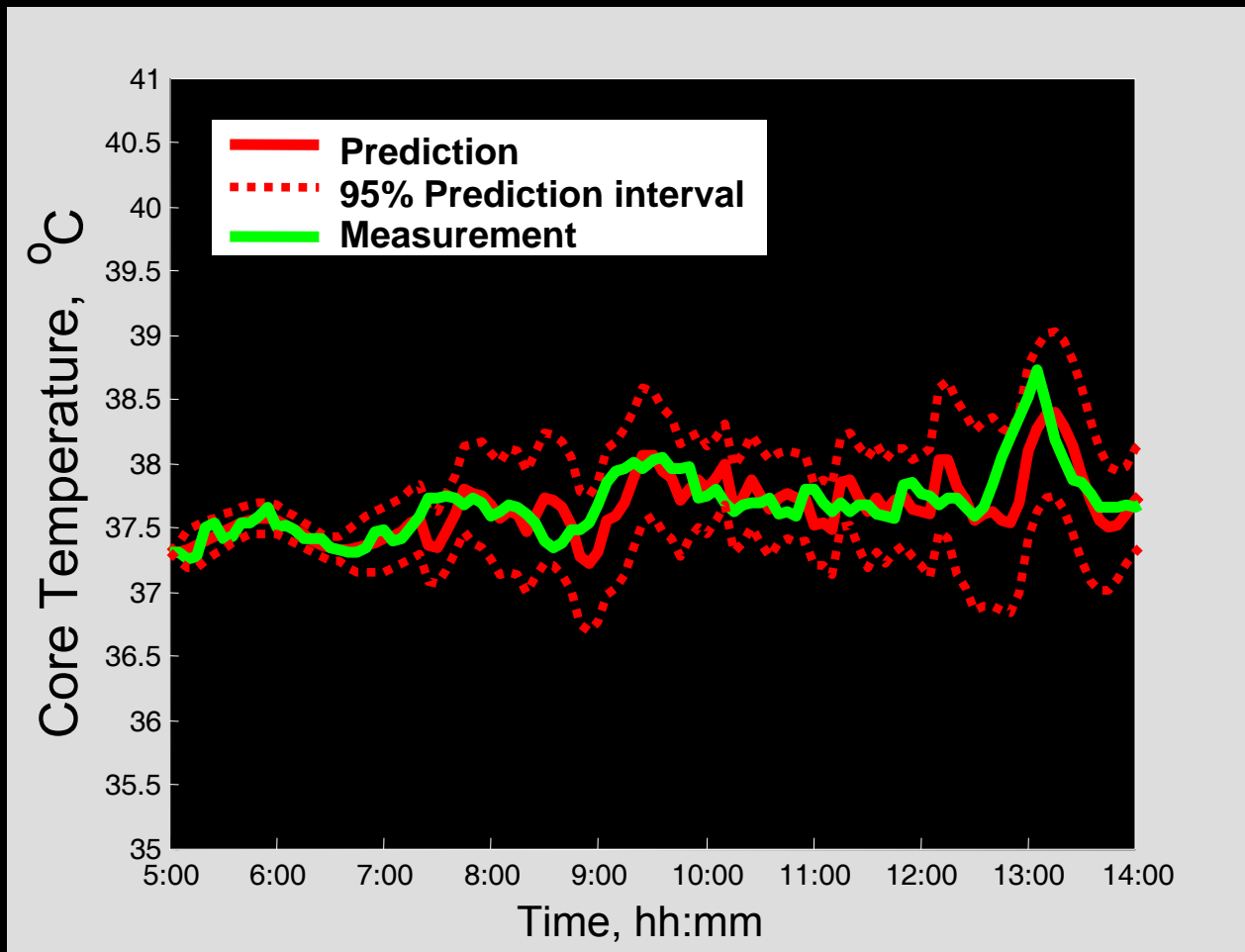
Measurement: Temperature pill (1-minute data)



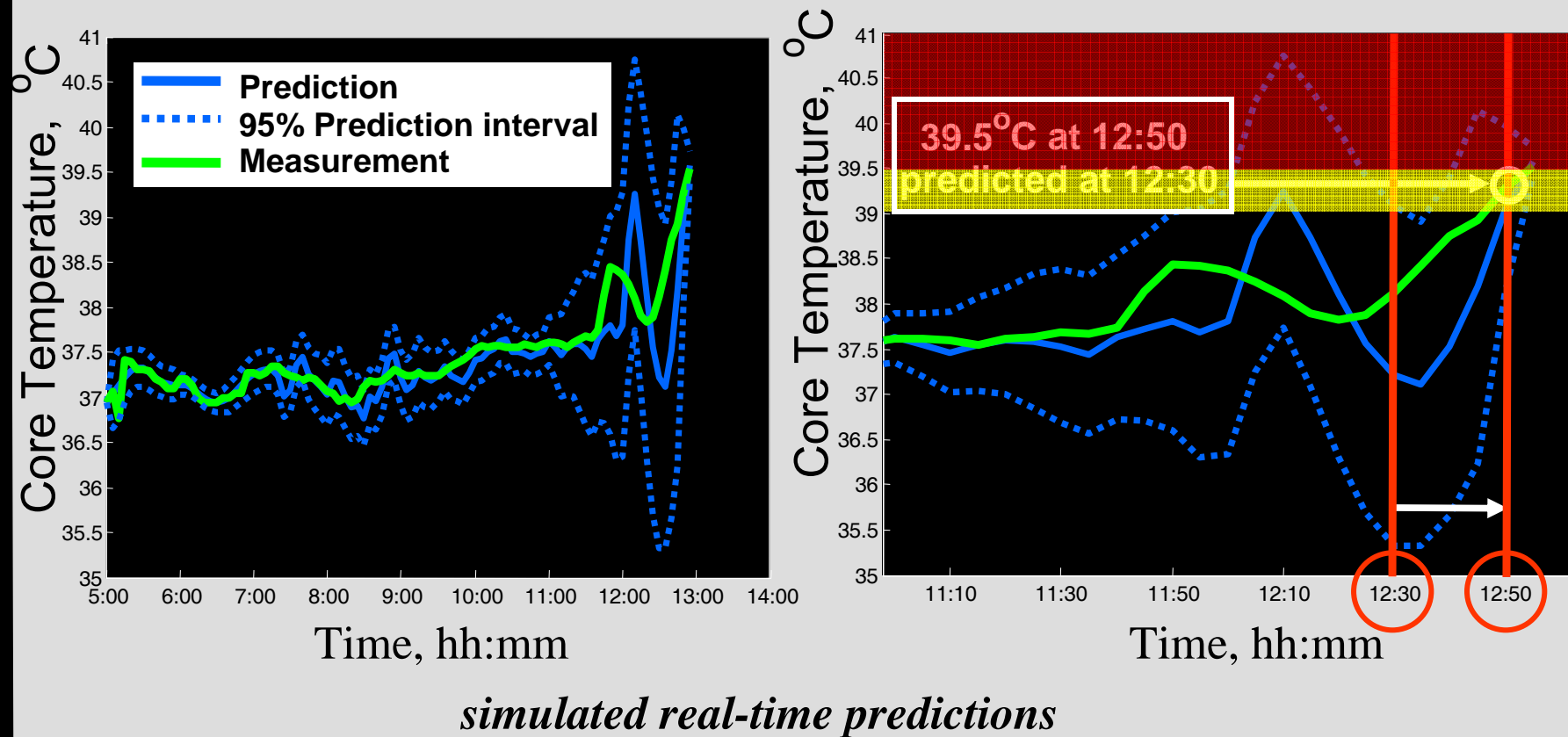
Joint Readiness Training Center, Ft. Polk, LA, Aug/01

- West Point **Cadet** and **Soldier** from 509th Infantry Regiment
- **Soldier** was very fit and heat acclimated
- **Cadet** was not as fit, not heat acclimated and was carrying a heavier load
- **Soldier's** model used to predict **Cadet's** temperature and vice versa

Cadet's Model Used to Predict Soldier's Core Temperature 20-min Ahead



Soldier's Model Used to Predict Cadet's Core Temperature 20-min Ahead

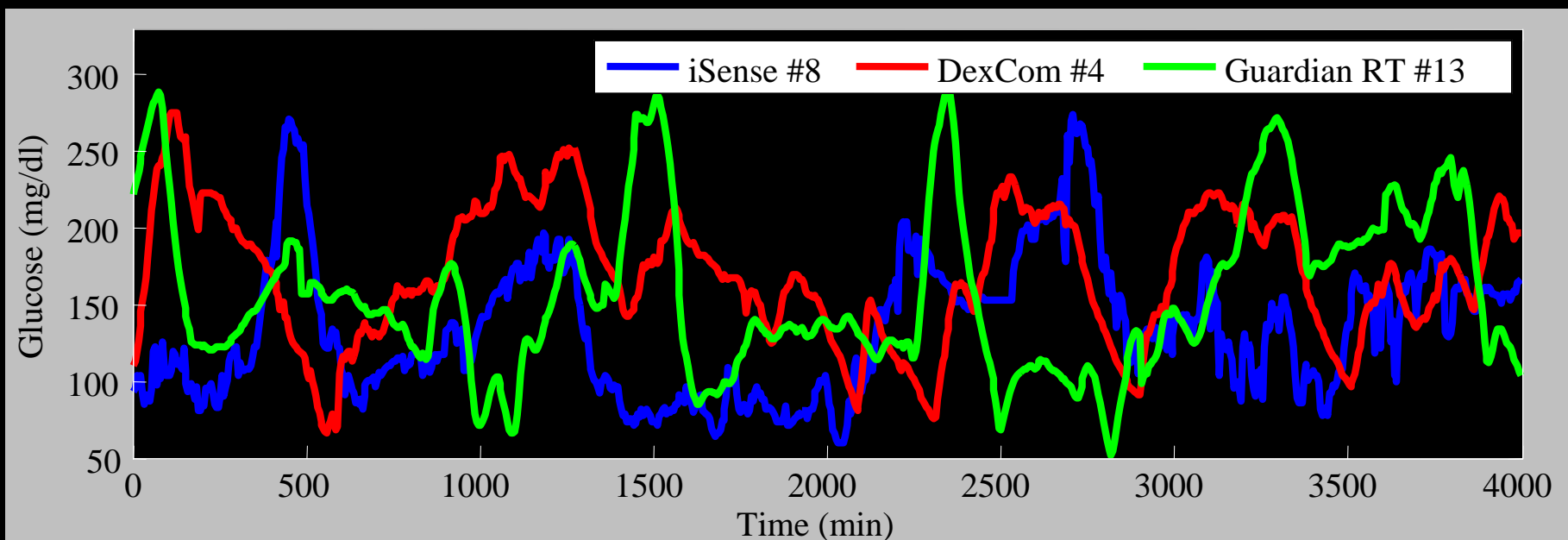


Gribok, Buller, and Reifman, *IEEE Trans. Biomed. Eng.*, in press
Gribok, Buller, Hoyt, and Reifman, under review

Glucose Prediction for Type 1 & 2 Diabetes

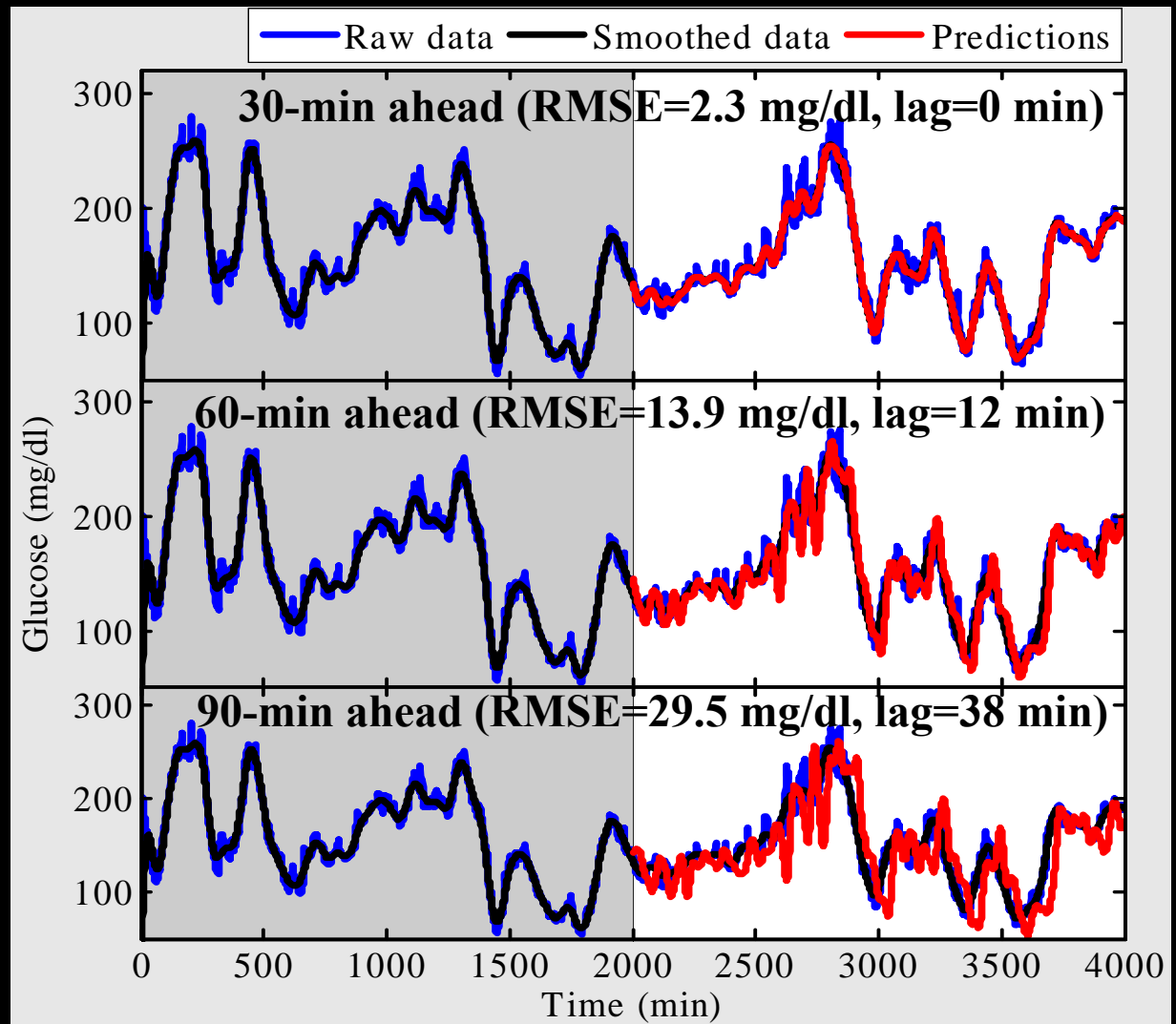
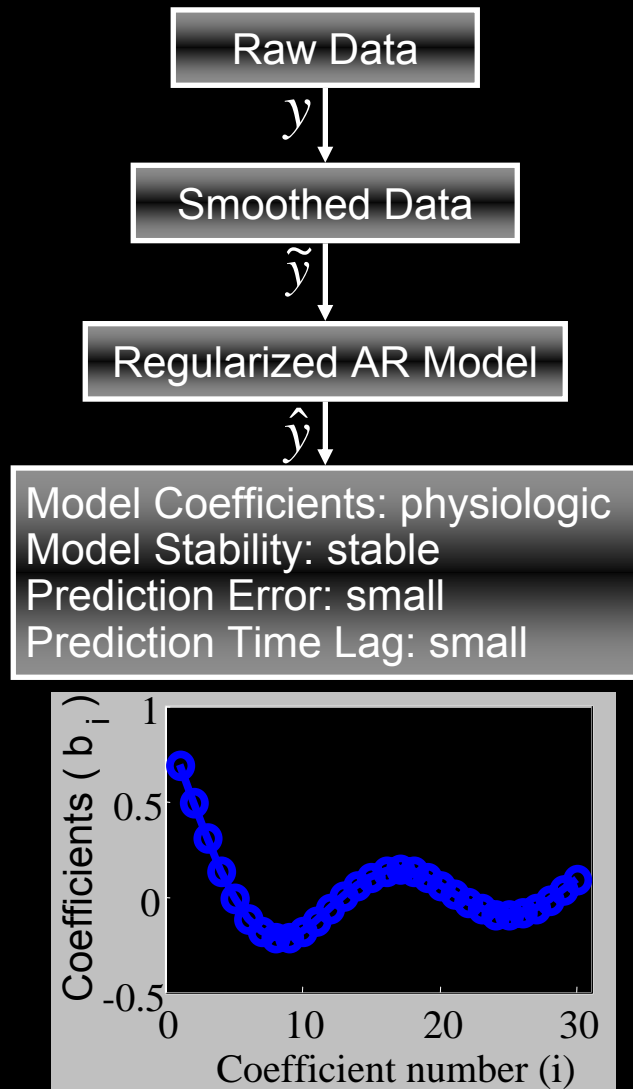
- *three studies using distinct continuous glucose monitoring (CGM) devices* -

CGM Device*	# of Subjects	Diabetes Type	Sampling Frequency (min)	Collection Time (days)
iSense	9	1	1	5
DexCom	7	2	5	56
Guardian RT	18	1	5	6



*Data provided by Ken Ward (iSense), Robert Vigersky (DexCom), Direcnet (Guardian RT)

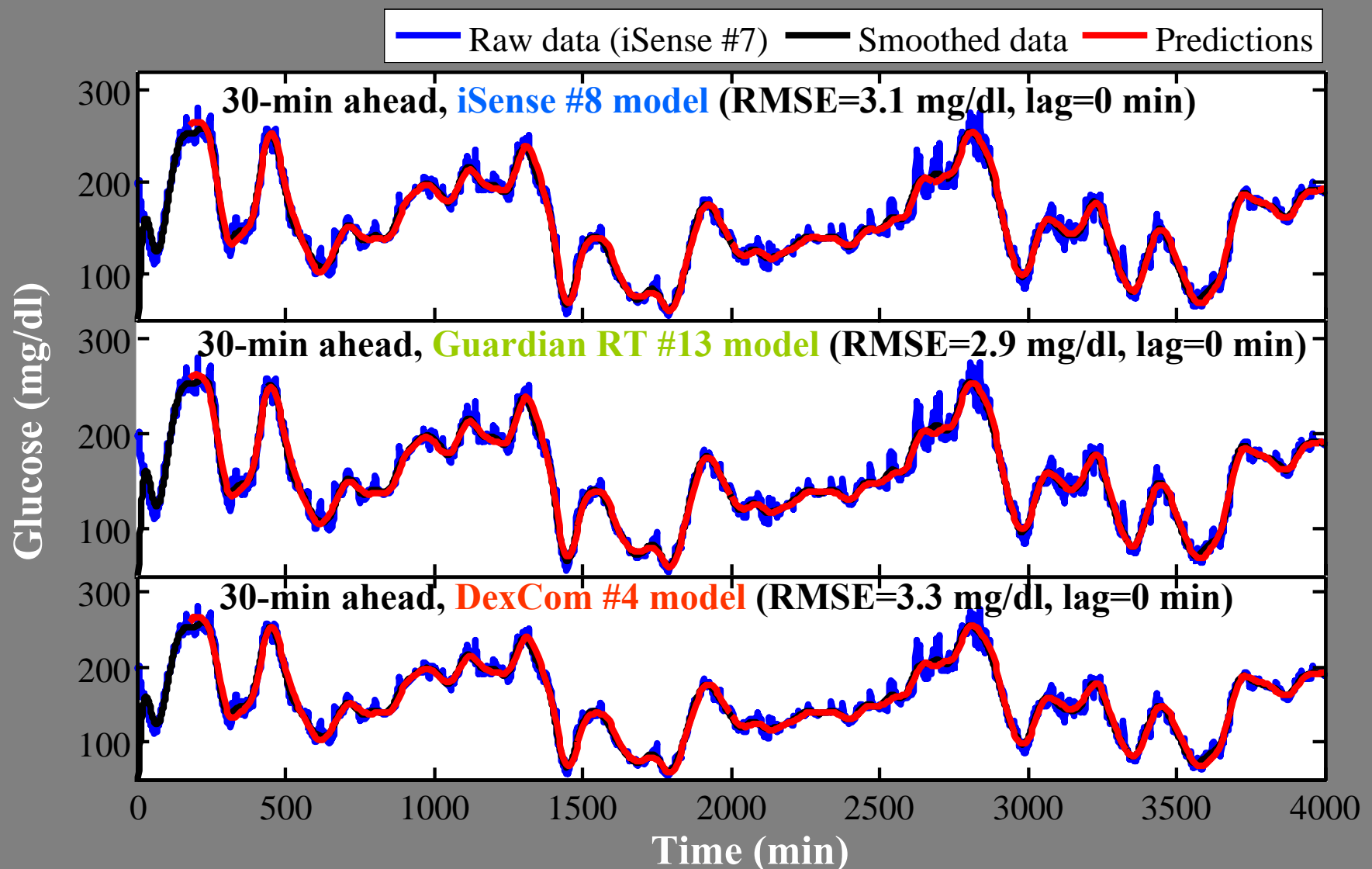
Glucose Prediction for iSense Subject #7



Reifman et al., *Diabetes Science & Technology*, 1, 478 (2007)

Gani et al., under review

Models from 3 Different Subjects Used for Glucose Prediction of iSense Subject #7



Universal Model

- *predictions across different subjects, devices, types of diabetes* -

iSense Testing Subject #	30-min Prediction Horizon (models based on different subjects/devices)					
	iSense Model (Avg. 8)		Guardian RT Model (Avg. 18)		DexCom Model (Avg. 7)	
	RMSE (mg/dl)	Lag (min)	RMSE (mg/dl)	Lag (min)	RMSE (mg/dl)	Lag (min)
1	2.3	1.3	2.2	0.8	2.2	2.1
2	3.4	0.0	3.1	0.0	3.3	0.0
3	3.7	0.0	3.5	0.0	3.7	0.0
4	3.2	1.3	3.0	1.7	3.2	5.0
5	4.1	0.0	3.9	0.0	3.9	0.0
6	3.8	0.0	3.6	0.0	3.8	0.0
7	3.0	0.0	2.9	0.0	3.0	0.0
8	3.3	0.0	3.2	0.0	3.2	0.0
9	2.5	0.0	2.5	0.0	2.5	0.0
Average	3.3	0.3	3.1	0.3	3.2	0.8

What's Next? Field Testing of Universal Model

$$y(t) = b_1 y(t-1) + b_2 y(t-2) + \dots + b_{30} y(t-30)$$



**Real-Time Body Core
Temperature Prediction**



Joint effort with Reed Hoyt's group (USARIEM)

*“All models are wrong,
some are useful.”*

George Box



QUESTIONS?

NCI-FREDERICK
DoD Biotechnology HPC
Software Applications Institute

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